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☐	L4	L3 and CD8	187
☐	L3	(hybrid or fus$) near3 tumor cell$	754
☐	L2	L1 and CD8	6
☐	L1	TBH or tumor B-cell hybrid	355

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NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements
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=> s CD8
L1 131390 CD8

=> s tumor B cell hybrid or TBH
L2 746 TUMOR B CELL HYBRID OR TBH

=> s l1 and l2
L3 14 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 6 DUP REM L3 (8 DUPLICATES REMOVED)

=> d bib abs 1-
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L4 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2006:135740 BIOSIS <<LOGINID::20070522>>
DN PREV200600137872
TI Safety and activity of DC- ***TBH*** vaccine.
AU Moviglia, Gustavo A. [Reprint Author]; Gaeta, C.; Varela, G.; Costanzo, H.; Farina, P.; Moviglia, M. T.; Bastos, F.; Merino, S.; Velloso, M. J.; Maranon, G.
CS Fdn Regina Mater, Buenos Aires, DF, Argentina
SO Journal of Immunotherapy, (NOV-DEC 2005) Vol. 28, No. 6, pp. 616-617. Meeting Info.: 20th Annual Scientific Meeting of the International-Society-for-Biological-Therapy-of-Cancer. Alexandria, VA, USA. November 10 -13, 2005. Int Soc Biol Therapy Canc.
ISSN: 1524-9557.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 22 Feb 2006
Last Updated on STN: 22 Feb 2006

L4 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 1999:47500 BIOSIS <<LOGINID::20070522>>
DN PREV199900047500
TI Modulating the antitumor immunity of MBT-2 murine bladder tumor bearing mice by postoperative administration of interferon-alpha.
AU Tzai, Tzong-Shin [Reprint author]; Shiau, Ai-Li; Wu, Chao-Liang; Chow, Nan-Haw; Tsai, Yuh-Shyan
CS Dep. Urol., Med. Coll., Natl. Cheng Kung Univ., 138 Sheng Li Road, Tainan, Taiwan
SO Anticancer Research, (Sept.-Oct., 1998) Vol. 18, No. 5A, pp. 3355-3361. print.
CODEN: ANTRD4. ISSN: 0250-7005.
DT Article
LA English
ED Entered STN: 10 Feb 1999
Last Updated on STN: 10 Feb 1999
AB This study was conducted mainly to investigate the effect of interferon-alpha (IFN-alpha) on the antitumor immunity of a tumor beating host (***TBH***) when postoperatively administrated with or without lethally irradiated autologous tumor cells. Using the C3H/He-MBT-2 murine bladder tumor model, a status of postoperative residual tumor was mimicked by rechallenging tumor cells 24 hours after resecting the day-17 tumor. Using immunohistochemical analysis we demonstrated that after treating with lethally irradiated MBT-2 tumor cells (IRMBT-2) + IL-2 cells of CD4+, ***CD8*** +, CD44+ and CD11b+ phenotypes prominently infiltrate the subcutaneous Local injection sites. In contrast, only scanty immune responding cells could be seen locally if treated with IRMBT-2 + IFN-alpha2b, albeit in the presence of interleukin-2 (IL-2). However, the spleens of D17TBM treated with IRMBT-2 + IFN-alpha2b contained the highest percentage of CD44+ memory T cells and cells of the CD11b phenotype; moreover, their natural killer (NK), lymphokine activated killer (LAK) and cytotoxic T lymphocytes (CTL) activities were significantly augmented. The results of in vivo tumor rechallenge revealed that administration of IFN-alpha, either alone or combined with IRMBT-2, could both effectively suppress the outgrowth of perioperative rechallenged tumor cells as well as prolong the survival of ***TBH*** . We conclude that despite the presence of autologous tumor vaccine, postoperative administration of IFN-alpha can further enhance the antitumor immunity of ***TBH*** and therefore can be an effective adjuvant therapy to improve the therapeutic results of surgery on a tumor bearing host.

L4 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2
AN 1995:317437 BIOSIS <<LOGINID::20070522>>
DN PREV199598331737
TI Adoptive transfer of ex vivo-activated memory T-cell subsets with cyclophosphamide provides effective tumor-specific chemoimmunotherapy of

advanced metastatic murine melanoma and carcinoma.
AU Gold, Jay E. [Reprint author]; Zachary, David T.; Osband, Michael E.
CS Mount Sinai Med. Cent., Div. Hematol., New York, NY 10029, USA
SO International Journal of Cancer, (1995) Vol. 61, No. 4, pp. 580-586.
CODEN: IJCNAW. ISSN: 0020-7136.
DT Article
LA English
ED Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995
AB Autolymphocyte therapy (ALT) is adoptive cellular therapy of neoplastic disease using ex vivo activation of autologous (human) or syngeneic (murine) lymphocytes from tumor-bearing hosts (***TBH***) by low doses of anti-CD3 monoclonal antibody (MAb) and a mixture of previously prepared autologous cytokines (T3CS). Ex vivo activation by T3CS without tumor antigen results in expansion of CD44+ (memory) T cells. These memory T cells (ALT cells) mediate in vivo anti-tumor specificity and with cyclophosphamide (CY) are capable of curing metastatic disease in murine ***TBH*** . To determine whether CY could enhance the effectiveness of CD4+ or ***CD8*** + subsets of ALT cells, C57BL/6J ***TBH*** with B16 melanoma or Lewis lung (3LL) carcinoma were treated with adoptive chemoimmunotherapy (ACIT) using CD4-depleted or ***CD8*** -depleted ALT cells and CY. ALT cells were derived from splenocytes of B16 or 3LL-***TBH*** and activated ex vivo with T3CS. Depletion of CD4+ or ***CD8*** + T cells was performed before or after activation with T3CS. B16- ***TBH*** or 3LL- ***TBH*** that received ACIT using CY with B16-derived or 3LL-derived ***CD8*** -depleted ALT cells, respectively, demonstrated cure of metastatic disease regardless of whether ***CD8*** + T cells were depleted before or after T3CS activation. B16 or 3LL-***TBH*** that received ACIT using CY with B16 or 3LL-derived CD4-depleted ALT cells also cured metastatic disease but only if CD4+ T cells were depleted after T3CS activation. Interleukin (IL)-2 added to pre-T3CS CD4-depleted ALT cells cultured with T3CS restored anti-tumor activity when combined with CY. ***TBH*** cured by ACIT using CY and ALT-cell subsets derived from syngeneic ***TBH*** with the identical tumor displayed tumor-specific immunity in rejecting a lethal challenge of identical but not reciprocal tumor. ***TBH*** given ACIT using CY and ALT-cell subsets derived from splenocytes of syngeneic ***TBH*** with reciprocal tumors rejected lethal challenges of both tumors. Tumor specificity measured by interferon (IFN)-gamma and 51Cr-release assays was demonstrated in pre- or post-T3CS/ ***CD8*** -depleted, post-T3CS/CD4-depleted and pre-T3CS + IL-2/CD4-depleted ALT-cell subsets. Our data demonstrate that ACIT using CY combined with ex vivo T3CS-activated CD44+ memory T-cell subsets conveys long-term tumor-specific immunity.

L4 ANSWER 4 OF 6 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 95251158 EMBASE <<LOGINID::20070522>>
DN 1995251158
TI Autolymphocyte therapy. III. Effective adjuvant adoptive cellular therapy with in vivo anti-tumor specificity against murine melanoma and carcinoma using ex-vivo-activated memory T-lymphocytes.
AU Gold J.E.; Masters T.R.; Osband M.E.
CS Department of Medicine, Mount Sinai Medical Center,New York, NY 10029, United States
SO Journal of Surgical Research, (1995) Vol. 59, No. 2, pp. 279-286. .
ISSN: 0022-4804 CODEN: JSGRA2
CY United States
DT Journal; Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 6 Sep 1995
Last Updated on STN: 6 Sep 1995
AB Autolymphocyte therapy (ALT) is adoptive cellular therapy of neoplastic disease based upon ex vivo activation of lymphocytes by either the supernatant derived from a previously prepared one-way mixed lymphocyte culture (MLC) or using low doses of the mitogenic monoclonal antibody OKT3 and a mixture of previously prepared cytokines (T3CS). We have previously demonstrated that nonspecific ex vivo activation of splenocytes from murine tumor-bearing hosts (***TBH***) using an MLC-supernatant or T3CS without the use of tumor antigen results in the expansion of the CD44+ (memory) T-cell subset. These CD44+ T-cells are the principal mediators of anti-tumor specificity in the ALT-cell population in advanced metastatic murine tumors and are able to protect against tumor challenge in healthy syngeneic mice (HSM). To determine if ALT is effective in an adjuvant setting, C57BL/6J splenocytes from HSM and ***TBH*** with B 16 melanoma or Lewis lung (3LL) carcinoma were activated ex vivo using T3CS. Mice were implanted with either B16 melanoma or 3LL carcinoma and then underwent surgical excision of tumor. Tumor-excised mice (TEM) then received small numbers (106) of ALT-cells derived from 3LL- ***TBH*** or B16- ***TBH*** splenocytes, HSM-derived ALT-cells, fresh splenocytes derived from 3LL- ***TBH*** or B16- ***TBH*** , or CD44-depleted ALT-cells. Significant anti-tumor activity as shown by prolonged survival (Day 100), cure of disease, and rejection of a local and systemic tumor rechallenge was demonstrated in 3LL-TEM that received 3LL- derived ALT-cells and in B16-TEM that received B16-derived ALT-cells. TEM that received HSM-derived ALT-cells, fresh ***TBH*** -derived splenocytes, or CD44- depleted ALT-cells demonstrated no greater anti-tumor effects than those treated with surgery alone. TEM that received ALT-cells from reciprocal ***TBH*** did not have increased survival or cure of disease over TEM treated by surgery alone, but were able to reject challenges of both tumors. These data suggest that effective adjuvant adoptive cellular therapy is possible using small numbers of ex vivo T3CS-activated splenocytes from murine ***TBH*** , that the anti-tumor effect is specific and dependent on memory T-cell infusion, and that this strategy may be effective in human patients in the adjuvant setting.

L4 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 3
AN 1994:213210 BIOSIS <<LOGINID::20070522>>
DN PREV199497226210
TI Tumor growth alters T cell and macrophage production of and responsiveness to granulocyte-macrophage colony-stimulating factor: Partial dysregulation through interleukin-10.
AU Walker, Thomas M.; Burger, Carol J.; Elgert, Klaus D. [Reprint author]
CS Microbiol. Immunol. Sect., Dep. Biol., Virginia Polytechnic Inst. State Univ., Blacksburg, VA 240651-0406, USA
SO Cellular Immunology, (1994) Vol. 154, No. 2, pp. 342-357.
CODEN: CLIMB8. ISSN: 0008-8749.
DT Article
LA English
ED Entered STN: 10 May 1994
Last Updated on STN: 10 May 1994
AB Tumor growth induces phenotypic and functional changes among splenic T cells and macrophages (M-vphi) that contribute to the immunosuppression observed in tumor-bearing hosts (***TBH***). These changes partly arise through alterations in immune cell production of and responsiveness to cytokines. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is an important T cell- and M-vphi-derived cytokine that is produced during normal host immunogenic challenge, but it's involvement during cancer is poorly defined. In contrast, interleukin-10 (IL-10) is an inhibitory cytokine that is produced by immune cells as a deactivation factor. IL-10 can disrupt GM-CSF synthesis and may be associated with tumor-induced changes in cytokine synthesis. We determined if tumor growth alters T-cell and M-vphi synthesis of and responsiveness to GM-CSF, and if these alterations occur because tumor growth heightens immune cell sensitivity to IL-10. Tumor growth significantly decreased T-cell synthesis of GM-CSF during activation by concanavalin A, and ***TBH*** T cells were more susceptible to GM-CSF synthesis inhibition by IL-10 than their normal host (NH) counterparts. This suppression was observed using both unseparated splenic lymphocyte preparations and purified CD4+ and ***CD8*** + T cells. Similarly, ***TBH*** MO (both splenic and peritonea)) produced less GM-CSF than NH M-vphi during activation by lipopolysaccharide. Tumor growth also altered major histocompatibility complex (MHC) class IL-M-vphi GM-CSF synthesis. ***TBH*** M-vphi were more susceptible to GM-CSF synthesis inhibition by IL-10 than their NH counterparts. Although ***TBH*** T cells demonstrate less proliferation than NH T cells during activation, tumor growth did not compromise T-cell responsiveness to GM-CSF. However, tumor growth did increase ***TBH*** T-cell susceptibility to inhibition of proliferation by IL-10. Tumor growth suppressed M-vphi responsiveness to GM-CSF, and IL-10 further decreased M-vphi responsiveness to GM-CSF. Collectively, these results suggest that T cell and M-vphi production of and responsiveness to GM-CSF is disrupted during tumor growth, and that ***TBH*** T cells and M-vphi are more susceptible to the suppressor activity of IL-10 than their NH counterparts.

L4 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 4
AN 1993:114368 BIOSIS <<LOGINID::20070522>>
DN PREV199395058468
TI Cytokines and suppressor macrophages cause tumor-bearing host ***CD8*** positive T cells to suppress recognition and allogeneic and syngeneic MHC class II molecules.
AU Walker, Thomas M.; Yurochko, Andrew D.; Burger, Carol J.; Elgert, Klaus D. [Reprint author]
CS Dep. Biol., Microbiol. Immunol. Sect., Va. Polytechnic Inst., State Univ., Blacksburg, Va. 24061-0406, USA
SO Journal of Leukocyte Biology, (1992) Vol. 52, No. 6, pp. 661-669.
CODEN: JLBIE7. ISSN: 0741-5400.
DT Article
LA English
ED Entered STN: 27 Feb 1993
Last Updated on STN: 27 Feb 1993
AB Quantitative and qualitative tumor-associated changes in T cell phenotype and function were identified in ***CD8*** + T cells. Tumor growth changed splenic CD4+/ ***CD8*** + T cell ratios and induced the appearance of more cells with the ***CD8*** + phenotype. In comparison to equal concentrations of normal host (NH) counterparts, tumor-bearing host (***TBH***) ***CD8*** + T cells were highly suppressive to allorecognition and autorecognition. Suppression was not due to quantitative reductions in CD4+ T cells, although minor qualitative differences were observed. Suppression appeared to be mediated partly by prostaglandin E-2 (PGE-2). Interferon-gamma (INF-gamma) and interleukin-4 (IL-4) contributed to ***TBH*** ***CD8*** + T cell-mediated suppression. Blocking studies using monoclonal antibodies (mAb) in conjunction with indomethacin suggested that cytokine networks involving IFN-gamma, IL-4, and PGE-2 were disrupted during tumor growth and promoted ***TBH*** ***CD8*** + T cell suppression. Alloresponses and autoresponses were significantly suppressed when ***TBH*** ***CD8*** + T cells mediated these reactions simultaneously with ***TBH*** Ia-macrophages. Inhibition of PGE-2 production was unable to reverse the

additive suppression caused by these two cell types. These results collectively suggest that tumor-induced changes in ***CD8*** + T cells lead to suppressed allorecognition and autorecognition through both soluble mediator molecules and cellular interactions.

=> s (hybrid or fus?) (3a) tumor cell?
L5 862 (HYBRID OR FUS?) (3A) TUMOR CELL?

=> s l5 and l1
L6 68 L5 AND L1

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 39 DUP REM L6 (29 DUPLICATES REMOVED)

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L7 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:829070 CAPLUS <<LOGINID::20070522>>
DN 145:436707
TI Apoptotic, necrotic, or ***fused*** ***tumor*** ***cells*** : An equivalent source of antigen for dendritic cell loading
AU Larmonier, Nicolas; Merino, Delphine; Nicolas, Alexandra; Cathelin, Dominique; Besson, Angelique; Bateman, Andrew; Solary, Eric; Martin, Francois; Katsanis, Emmanuel; Bonnotte, Bernard
CS INSERM U517, IFR 100, Faculty of Medicine and Pharmacy, Dijon, 21079, Fr.
SO Apoptosis (2006), 11(9), 1513-1524
CODEN: APOPFN; ISSN: 1360-8185
PB Springer
DT Journal
LA English
AB The identification of the most efficient strategy for tumor antigen loading of dendritic cells (DCs) remains a challenge in cancer immunotherapy protocols. Autologous dead tumor cells have been demonstrated to constitute an acceptable source of multiple tumor-assocd. antigens (TAA) to pulse DCs. However the optimal approach for inducing cell death that would lead to effective endocytosis and activation of DCs remains controversial. In this study we have induced and defined 3 distinct mechanisms of tumor cell death (apoptosis, necrosis and fusion-mediated cell death), and investigated their differential effects on DCs. Bone marrow-derived DCs demonstrated comparable uptake of primary apoptotic, necrotic, or ***fused*** dead ***tumor*** ***cells*** . Furthermore, the distinct modes of cancer cell death had analogous potential in activating the transcription factors NF-.kappa.B and STAT1 and in maturing DCs, resulting in an equally effective stimulation of immune T cells. The current study therefore provides further informations on the use of dead whole tumor cells as antigen sources for effective active anti-cancer immunotherapy.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:211133 CAPLUS <<LOGINID::20070522>>
DN 145:165008
TI Dendritoma vaccination combined with low dose interleukin-2 in metastatic melanoma patients induced immunological and clinical responses
AU Wei, Yanzhang; Sticca, Robert P.; Holmes, Lillia M.; Burgin, Kelly E.; Li, Jinhua; Williamson, Jane; Evans, Lyndon; Smith, Samuel J.; Stephenson, Joseph J.; Wagner, Thomas E.
CS Oncology Research Institute and the Cancer Treatment Center, Greenville Hospital System, USA
SO International Journal of Oncology (2006), 28(3), 585-593
CODEN: IJONES; ISSN: 1019-6439
PB International Journal of Oncology
DT Journal
LA English
AB A pilot clin. trial using dendritomas, purified hybrids from the ***fusion*** of dendritic/ ***tumor*** ***cells*** combined with a low dose of IL-2, in metastatic melanoma patients was conducted in order to det. its safety and potential immunol. and clin. responses. Ten metastatic melanoma patients were enrolled into this study. Dendritoma vaccines were created by fusing dendritic cells stained with green fluorescent dye with irradiated autologous tumor cells stained with red fluorescent dye and purifying the hybrids using immediate fluorescent-activated cell sorting. Initial vaccine was given s.c. and followed by IL-2 in serially elevated doses from 3-9 million units/m2 for 5 days. Repeated vaccinations were administered without IL-2, at 3-mo intervals for a max. of 5 times. Immune reactions were measured by the increase of interferon-.gamma. (IFN-.gamma.) expressing T cells. Vaccine doses ranged from 250,000 to 1,000,000 dendritomas. There was no grade 2 or higher toxicity directly attributable to the vaccine. All patients experienced toxicity due to IL-2 administration (9-grade 2, 3-grade 3, 1-grade 4). Eight of nine evaluable patients demonstrated immunol. reactions by increased IFN-.gamma. expressing T cells. One patient developed partial response at 12 wk after the first vaccine. Nine months later, this patient achieved a complete response. In addn., two patients had stable disease for 9 and 4 mo, resp.; one patient had a mixed response. Our findings demonstrated that dendritoma vaccines with a low dose of IL-2 can be safely administered to patients with metastatic melanoma and induce immunol. and clin. responses.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 1
AN 2007:151711 BIOSIS <<LOGINID::20070522>>
DN PREV200700158626
TI Comparative analysis of DC ***fused*** with ***tumor*** ***cells*** or transfected with tumor total RNA as potential cancer vaccines against hepatocellular carcinoma.
AU Zhang, Hong-Mei [Reprint Author]; Zhang, Li-Wang; Liu, Wen-Chao; Cheng, Jie; Si, Xiao-Ming; Ren, Jun
CS Fourth Mil Med Univ, Xijing Hosp, Ctr Clin Oncol, 15 Chang Le W Rd, Xian 710032, Peoples R China
zhm@fmmu.edu.cn
SO CYTOTHERAPY, (DEC 2006) Vol. 8, No. 6, pp. 580-588.
ISSN: 1465-3249.
DT Article
LA English
ED Entered STN: 7 Mar 2007
Last Updated on STN: 7 Mar 2007
AB Background DC vaccination with the use of tumor cells provides the potential to generate a polyclonal immune response to multiple known and unknown tumor Ag. Our study comparatively analyzed DC ***fused*** with ***tumor*** ***cells*** or transfected with tumor total RNA as potential cancer vaccines against hepatocellular carcinoma (HCC).Methods Immature DC generated from PBMC of patients with HCC were fused with HepG2-GFP (HepG2 cell line transfected stably with plasmid pEGFP-C3) cells or transfected with their total RNA. Matured DC were used to stimulate autologous T cells, and the resultant Ag-specific effector T cells were analyzed by IFN-gamma ELISPOT assay.Results DC were capable of further differentiation into mature DC after fusion with HepG2-GFP cells or transfection with HepG2-GFP cell total RNA, and were able to elicit specific T-cell responses in vitro. Both methods of Ag loading could result in stimulating CD4(+) and ***CD8*** (+) T cells, but with the indication that fusion loading was more efficient than RNA loading in priming the Th1 response, while RNA loading was more effective in CTL priming.Discussion Our results indicate that DC ***fused*** with ***tumor*** ***cells*** or transfected with tumor total RNA represent promising strategies for the development of cancer vaccines for treatment of HCC. They may have potential as an adjuvant immunotherapy for patients with HCC.

L7 ANSWER 4 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2
AN 2006:528021 BIOSIS <<LOGINID::20070522>>
DN PREV200600527345
TI Induction of cytotoxic T lymphocytes against human cancer cell lines using dendritic cell-tumor cell hybrids generated by a newly developed electrofusion technique.
AU Imura, Kenichiro; Ueda, Yuji [Reprint Author]; Hayashi, Takashi; Itoh, Tsuyoshi; Shimizu, Keiji; Tamai, Hidemasa; Yano, Yutaro; Naito, Kei; Kohara, Junji; Nakane, Kazuki; Matsuura, Yuko; Takeda, Atsuko; Takeda, Takahisa; Kawai, Keiichi; Yamagishi, Hisakazu
CS Kyoto Prefectural Univ Med, Dept Surg, Div Digest Surg, Kamigyo Ku, 465 Kajii Cho, Kyoto 6028566, Japan
yueda@koto.kpu-m.ac.jp
SO International Journal of Oncology, (SEP 2006) Vol. 29, No. 3, pp. 531-539.
ISSN: 1019-6439.
DT Article
LA English
ED Entered STN: 12 Oct 2006
Last Updated on STN: 12 Oct 2006
AB Recently, dendritic cells (DCs) and DC-tumor cell hybrids (DC-tumor hybrids) have been used for cancer vaccine therapy in a clinical trial. DC-tumor hybrids combine the potent antigen-presenting capacity of DCs with the ability to present all tumor antigens expressed on tumor cells to T cells. We used DC-tumor hybrids as stimulator cells to induce tumor-specific cytotoxic T lymphocytes (CTLs) in vitro. DC-tumor hybrids were generated from human monocyte-derived DCs and human cancer-cell lines (GT3TKB, lung cancer; GCIY, gastric cancer) by our newly developed electro-fusion technique, established and refined with the use of mouse cells. To evaluate the capacity of DC-tumor hybrids generated by our method to induce tumor antigen-specific CTLs, we performed a cytotoxic assay and an interferon-gamma release assay using ***CD8*** -dominant effector lymphocytes induced by them. DC-tumor hybrids more effectively induced tumor-specific primary T-cell response than did stimulation with DCs co-cultured with irradiated tumor cells overnight, irradiated tumor cells alone, or a mixture of DCs and irradiated tumor cells. DC-tumor hybrids were generated at a high fusion rate by our electro-fusion technique. When CTLs were induced by DC-tumor hybrids in vitro, the high fusion rate did not contribute to the induction of CTLs with increased tumor-specific cytotoxicity. The addition of interleukin-12 to the culture medium did not augment the cytotoxicity of CTLs. Overall, our results suggest that DC-tumor hybrids effectively induce human tumor-specific CTLs and may thus be applicable for clinical trials of adoptive immunotherapy.

L7 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:997964 CAPLUS <<LOGINID::20070522>>
DN 146:5954
TI Dendritic cells as potential adjuvant for immunotherapy in adrenocortical carcinoma
AU Papewalis, Claudia; Fassnacht, Martin; Willenberg, Holger S.; Domberg, Julia; Fenk, Roland; Rohr, Ulrich-Peter; Schinner, Sven; Bornstein, Stefan R.; Scherbaum, Werner A.; Schott, Matthias
CS Department of Endocrinology, Diabetes and Rheumatology, University Hospital Duesseldorf, Duesseldorf, Germany
SO Clinical Endocrinology (Oxford, United Kingdom) (2006), 65(2), 215-222
CODEN: CLECAP; ISSN: 0300-0664
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB Objective Adrenocortical carcinoma (ACC) is a rare malignancy assocd. with a dismal prognosis. Dendritic cells (DCs) are professional antigen-presenting cells leading to an antitumor immune response. The aim of this study was to elaborate two methods of antigen delivery to DCs and to evaluate an immunotherapy protocol in ACC patients. Design/patients Autologous DCs were pulsed with autologous tumor lysate (TL). ***Fusion*** of DCs with ***tumor*** ***cells*** was based on a polyethylene glycol method. Two patients with metastasized hypersecretory ACC were vaccinated twice. Measurements In vitro data were quantified by measurement of PBMC (peripheral blood mononuclear cell) responses and cytokine secretion and by flow cytometry analyses. Clin. response was monitored by CT scan of tumor mass and measurement of angiogenic factors. Results The max. loading of TL was obtained at 24 h as 48.2% (.+-.26.8%) of DCs were TL-pos. The DC/ ***tumor*** ***cell*** ***fusion*** efficacy was .apprx.45% as shown by double pos. staining for ACTH receptor and DC-specific CD83. In vivo DC vaccination resulted in pos. delayed-type hypersensitivity skin reactions reflecting specific memory T-lymphocyte reaction. In vitro analyses revealed specific T-cell proliferation in patient 1 (stimulation index: 5.7 compared to pretreatment) and induction of cytotoxic granzyme B secreting T cells in patient 2 (0.41% ***CD8*** + cells vs. 0.06% pretreatment) as indicators of specific cytotoxic T cells. Although angiogenic serum markers could be stabilized, no impact on tumor growth could be obsd. Conclusion Our data demonstrate that autologous dendritic cells induce antigen-specific Th1 immunity in adrenocortical carcinoma. The clin. outcome, however, was not improved in the patients studied here.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:471830 CAPLUS <<LOGINID::20070522>>
DN 143:25045
TI Listeria ActA fusion proteins for enhancing the immunogenicity of antigens
IN Paterson, Yvonne; Peters, Christian; Gunn, George
PA Trustees of the University of Pennsylvania, USA
SO U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 239,703, abandoned.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 9

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005118184	A1	20050602	US 2004-835662	20040430
US 2002028206	A1	20020307	US 2000-537642	20000329
US 6855320	B2	20050215		
US 2002025323	A1	20020228	US 2000-735450	20001213
US 6767542	B2	20040727		
US 2006210540	A1	20060921	US 2006-373528	20060313
US 2006205067	A1	20060914	US 2006-376564	20060316
US 2006204516	A1	20060914	US 2006-376572	20060316
US 2006269561	A1	20061130	US 2006-415271	20060502
PRAI US 2000-537642	A2	20000329		
US 2000-735450	A2	20001213		
US 2002-239703	B2	20020924		
US 1994-336372	A2	19941108		
US 2000-535212	A2	20000327		
WO 2001-US9736	A	20010326		
US 2003-441851	A2	20030520		
US 2003-239703	A2	20030807		
US 2004-835662	A1	20040430		
US 2004-949667	A2	20040924		
US 2005-223945	A2	20050913		
US 2006-373528	A2	20060313		

AB The authors disclose the immunogenicity of an antigen is enhanced via fusion to the Listerial protein ActA. The present invention further encompasses Listeria vaccine strains for enhancing the immunogenicity of an antigen. In one example, the authors demonstrate an enhanced ***CD8*** + T-cell response against lung ***tumor*** ***cells*** by a ***fusion*** protein of HPV16 E7 with ActA.

L7 ANSWER 7 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
AN 2005:1191221 CAPLUS <<LOGINID::20070522>>
DN 144:466205
TI Dendritic Cells Fused with Allogeneic Colorectal Cancer Cell Line Present Multiple Colorectal Cancer-Specific Antigens and Induce Antitumor Immunity against Autologous Tumor Cells
AU Koido, Shigeo; Hara, Eiichi; Homma, Sadamu; Torii, Akira; Toyama, Yoichi; Kawahara, Hidejiro; Watanabe, Michiaki; Yanaga, Katsuhiko; Fujise, Kiyotaka; Tajiri, Hisao; Gong, Jianlin; Toda, Gotaro
CS Department of Internal Medicine, Division of Gastroenterology and Hepatology, The Jikei University School of Medicine, Chiba, 277-8564, Japan
SO Clinical Cancer Research (2005), 11(21), 7891-7900
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB The aim of antitumor immunotherapy is to induce CTL responses against autologous tumors. Previous work has shown that fusion of human dendritic cells and autologous tumor cells induce CTL responses against autologous tumor cells in vitro. However, in the clin. setting of patients with colorectal carcinoma, a major difficulty is the prepn. of sufficient amts. of autologous tumor cells. In the present study, autologous dendritic cells from patients with colorectal carcinoma were ***fused*** to allogeneic colorectal ***tumor*** ***cell*** line, COLM-6 (HLA-A2-/HLA-24-), carcinoembryonic antigen (CEA)+, and MUC1+ as an alternative strategy to deliver shared colorectal carcinoma antigens to dendritic cells. Stimulation of autologous T cells by the fusion cells generated with autologous dendritic cells (HLA-A2+ and/or HLA-A24+) and allogeneic COLM-6 resulted in MHC class I- and MHC class II-restricted proliferation of CD4+ and ***CD8*** + T cells, high levels of IFN-.gamma. prodn. in both CD4+ and ***CD8*** + T cells, and the simultaneous induction of CEA- and MUC1-specific CTL responses restricted by HLA-A2 and/or HLA-A24. Finally, CTL induced by dendritic cell/allogeneic COLM-6 fusion cells were able to kill autologous colorectal carcinoma by HLA-A2- and/or HLA-A24-restricted mechanisms. The demonstration of CTL activity against shared tumor-assocd. antigens using an allogeneic tumor cell line, COLM-6, provides that the presence of alloantigens does not prevent the development of CTL with activity against autologous colorectal carcinoma cells. The fusion of allogeneic colorectal carcinoma cell line and autologous dendritic cells could have potential applicability to the field of antitumor immunotherapy through the cross-priming against shared tumor antigens and provides a platform for adoptive immunotherapy.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2005288490 EMBASE <<LOGINID::20070522>>
TI Dendritic cells: Activation and maturation - Applications for cancer immunotherapy.
AU Sheng K.-C.; Pietersz G.A.; Wright M.D.; Apostolopoulos V.
CS V. Apostolopoulos, The Austin Research Institute, Immunology and Vaccine Laboratory, Studley Road, Heidelberg, Vic. 3084, Australia. v.apostolopoulos@ari.unimelb.edu.au
SO Current Medicinal Chemistry, (2005) Vol. 12, No. 15, pp. 1783-1800. .
Refs: 179
ISSN: 0929-8673 CODEN: CMCHE7
CY Netherlands
DT Journal; General Review
FS 016 Cancer
022 Human Genetics
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LA English
SL English
ED Entered STN: 14 Jul 2005
Last Updated on STN: 14 Jul 2005
AB There is an increasing number of studies utilizing dendritic cell (DC) based therapies for cancer. With a powerful antigen-presentation capability, DCs have the potential to overcome tumor tolerance and induce anti-tumor immunity, when loaded with tumor antigens. In order to optimize this approach, methods have aimed to enhance immunopotency of therapeutic DCs. A thorough understanding of DC immunobiology would accelerate this process and provide advantageous procedures to increase anti-tumor responses. This review contains an analysis of recent advances on DC subsets, phenotypic characterization, localization, surface receptors and their ligands. The events of immune induction via DCs, involving initial recognition and uptake of antigens, migration, subsequent activation and maturation are revisited. Furthermore, the current methods used for DC-based cancer immunotherapy, including DCs pulsed with tumor antigens in forms of DNA, RNA, peptides, proteins and lysates, or DCs ***fused*** with ***tumor*** ***cells*** are summarized. Respective preclinical and clinical trials are in progress and hold promise for developing effective cancer vaccines. .COPYRGT. 2005 Bentham Science Publishers Ltd.

L7 ANSWER 9 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1255052 CAPLUS <<LOGINID::20070522>>
DN 144:348663
TI Fusion vaccine therapy by IL-2-gene-transduced dendritic cells and tumor cells
AU Ogawa, Fujio; Iinuma, Hidae; Iwasaki, Kota; Tamura, Junko; Kumagai, Harumi; Inaba, Tsuyoshi; Fukushima, Ryouji; Okinaga, Kota

CS Dept. of Surgery, Teikyo University School of Medicine, Itabashi-ku, Tokyo, 173-8605, Japan
SO Gan to Kagaku Ryoho (2005), 32(11), 1580-1582
CODEN: GTKRDX; ISSN: 0385-0684
PB Gan to Kagaku Ryohosha
DT Journal
LA Japanese
AB We evaluated the usefulness of fusion vaccine prepd. from IL-2-gene-transduced splenic dendritic cells (DCs) and fibrosarcoma tumor cells (QRsP) in treating of lung metastasis. The IL-2 or LacZ gene was transferred into spleen-derived DCs using an adenoviral vector. Irradiated QRsP ***tumor*** ***cells*** were ***fused*** with IL-2 gene transduced DCs (fusion/IL-2) or LacZ gene transduced DCs (fusion/LacZ) by polyethyleneglycol. These fusion cells expressed major histocompatibility complex (MHC) class I and MHC class II, CD86, CD11c and ***CD8*** .alpha.. IFN-.gamma. and cytotoxic T lymphocyte (CTL) activity of splenic lymphocytes in mice vaccinated with fusion cells increased significantly as compared with those of DC or tumor cells vaccinated mice. CTL levels in fusion/IL-2-vaccinated mice were higher than that in fusion/LacZ-vaccinated mice. The no. of lung metastasis in the fusion/IL-2 or fusion/LacZ-vaccinated mice was significantly lower than that in mice vaccinated with DCs, tumor or PBS. The introduction of the IL-2 gene into fusion cells produced more potent therapeutic effects. Our results suggest that the fusion cells prepd. from IL-2 gene transduced spleen derived DCs and tumor cells have the ability to induce therapeutic effect against lung metastasis.

L7 ANSWER 10 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 4
AN 2005:490650 BIOSIS <<LOGINID::20070522>>
DN PREV200510281709
TI Active immunotherapy for advanced intracranial murine tumors by using dendritic cell- ***tumor*** ***cell*** ***fusion*** vaccines.
AU Kjaergaard, Jorgen; Wang, Li-Xin; Kuriyama, Hideyuki; Shu, Suyu; Plautz, Gregory E. [Reprint Author]
CS Cleveland Clin Fdn, Surg Res Ctr, 9500 Euclid Ave,FF5, Cleveland, OH 44195 USA
plautzg@ccf.org
SO Journal of Neurosurgery, (JUL 2005) Vol. 103, No. 1, pp. 156-164.
CODEN: JONSAC. ISSN: 0022-3085.
DT Article
LA English
ED Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005
AB Object. Immunotherapy for malignant brain tumors by active immunization or adoptive transfer of tumor antigen-specific T lymphocytes has the potential to make up for some of the limitations of current clinical therapy. In this study, the authors tested whether active immunotherapy is curative in mice bearing advanced, rapidly progressive intracranial tumors.Methods. Tumor vaccines were created through electrofusion of dendritic cells (DCs) and irradiated tumor cells to form multinucleated heterokaryons that retained the potent antigen processing and costimulatory function of DCs as well as the entire complement of tumor antigens. Murine hosts bearing intracranial GL261 glioma or MCA 205 fibrosarcoma were treated with a combination of local cranial radiotherapy, intrasplenic vaccination with DC/tumor fusion cells, and anti-OX40R (CD 134) monoclonal antibody (mAb) 7 days after tumor inoculation.Whereas control mice had a median survival of approximately 20 days, the treated mice underwent complete tumor regression that was immunologically specific. Seven days after vaccination treated mice demonstrated robust infiltration of CD4(+) and ***CD8*** (+) T cells, which was exclusively confined to the tumor without apparent neurological toxicity. Cured mice survived longer than 120 days with no evidence of tumor recurrence and resisted intracranial tumor challenge.Conclusions. These data indicate a strategy to achieve an antitumor response against tumors in the central nervous system that is highly focused from both immunological and anatomical perspectives.

L7 ANSWER 11 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 5
AN 2004:324138 BIOSIS <<LOGINID::20070522>>
DN PREV200400324433
TI Development of antigen-specific ***CD8*** + CTL in MHC class I-deficient mice through CD4 to ***CD8*** conversion.
AU Tanaka, Yasuhiro; Koido, Shigeo; Xia, Jianchuan; Ohana, Masaya; Liu, Chunlei; Cote, Gregory M.; Sawyer, Douglas B.; Calderwood, Stuart; Gong, Jianlin [Reprint Author]
CS Sch MedDept Med, Boston Univ, 650 Albany St,Room 309, Boston, MA, 02118,
USA
jgong@bumc.bu.edu
SO Journal of Immunology, (June 15 2004) Vol. 172, No. 12, pp. 7848-7858.
print.
ISSN: 0022-1767 (ISSN print).
DT Article
LA English
ED Entered STN: 21 Jul 2004
Last Updated on STN: 21 Jul 2004
AB ***CD8*** + CTL are the predominant tumoricidal effector cells. We find, however, that MHC class I-deficient mice depleted of ***CD8*** + T cells are able to mount an effective antitumor immunity after immunization with ***fused*** dendritic/ ***tumor*** ***cells*** . Such immunity appears to be mediated by the generation of phenotypic and functional ***CD8*** + CTL through CD4+ to ***CD8*** + conversion, which we have demonstrated at the single cell level. CD4+ to ***CD8*** + conversion depends on effective in vivo activation and is promoted by CD4+ T cell proliferation. The effectiveness of this process is shown by the generation of antitumor immunity through adoptive transfer of primed CD4 T cells to provide protection against tumor cell challenge and to eliminate established pulmonary metastases.

L7 ANSWER 12 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2004192074 EMBASE <<LOGINID::20070522>>
TI In vitro antitumor immune response induced by fusion of dendritic cells and colon cancer cells.
AU Xu F.; Ye Y.-J.; Wang S.
CS Prof. S. Wang, Division of Surgical Oncology, People's Hospital, Peking University, 100044 Beijing, China. bronson_xu@yahoo.com.cn
SO World Journal of Gastroenterology, (15 Apr 2004) Vol. 10, No. 8, pp. 1162-1166. .
Refs: 27
ISSN: 1007-9327 CODEN: WJGAF2
CY China
DT Journal; Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
048 Gastroenterology
LA English
SL English
ED Entered STN: 20 May 2004
Last Updated on STN: 20 May 2004
AB Aim: The prevention of recurrence of colon cancer (CC) after operation is very important for improvement of the prognosis of CC patients, especially those with micro-metastasis. The generation of fused cells between dendritic cells (DCs) and tumor cells maybe an effective approach for tumor antigen presentation in immunotherapy. In this study, we fused human colon caner SW480 cells and human peripheral blood - derived DCs to induce an antitumor activity against human CC. Methods: CC SW480 cells and human peripheral blood - derived DCs were fused with 500 mL/L polyethylene glycol (PEG). Results: The specific T cell responses activated by fusion cells (FCs), were observed. About 100 mL/L to 160 mL/L of the PEG-treated non-adherent cells with fluorescences were considered to be dendritomas that highly expressed the key molecules for antigen presentation in our five cases. In vitro studies showed that fusions effectively activated ***CD8*** (+) T lymphocytes to secrete interferon-.gamma.. The early apoptotic ratio of the colon cancer SW480 cells was higher than that of controls, which was affected by cytotoxic T lymphocytes (CTLs) stimulated by dendritomas. Conclusion: The data indicate that ***fusion*** of ***tumor*** ***cells*** with DCs is an attractive strategy to induce tumor rejection. Copyright .COPYRGT. 2004 by The WJG Press.

L7 ANSWER 13 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 6
AN 2005:54879 BIOSIS <<LOGINID::20070522>>
DN PREV200500055273
TI Strategies for antigen choice and priming of dendritic cells influence the polarization and efficacy of antitumor T-cell responses in dendritic cell-based cancer vaccination.
AU Galea-Lauri, Joanna [Reprint Author]; Wells, James W.; Darling, David; Harrison, Phillip; Farzaneh, Farzin
CS Rayne InstGKT Sch MedDept Mol Med, Univ London Kings Coll, 123 Coldharbour
Lane, London, SE5 9NU, UK
joanna.galea-lauri@kcl.ac.uk
SO Cancer Immunology Immunotherapy, (November 2004) Vol. 53, No. 11, pp. 963-977. print.
CODEN: CIIMDN. ISSN: 0340-7004.
DT Article
LA English
ED Entered STN: 3 Feb 2005
Last Updated on STN: 3 Feb 2005
AB Dendritic cells (DCs) primed with tumor antigens (Ags) can stimulate tumor rejection. This study was aimed at evaluating the polarization of T-cell responses using various DC Ag-priming strategies for vaccination purposes. DCs cocultured with irradiated "apoptotic" ***tumor*** ***cells*** , DC-tumor ***fusions*** , and DCs pulsed with freeze-thaw tumor lysate Ags served as Ag-primed DCs, with EG7 tumor cells (class II negative) expressing OVA as the model Ag. DCs loaded with class I- and class II-restricted OVA synthetic peptides served as controls. Primed DCs were assessed by the in vitro activation of B3Z OVA-specific ***CD8*** T cells and the proliferation of OVA-specific ***CD8*** and CD4 T cells from OT-I and OT-II TCR transgenic mice, respectively. In vivo responses were measured by tumor regression following treatment with Ag-primed DCs and by CTL assays. Quantification of IL-2, IL-4, IL-5, IFN-gamma, and TNF-alpha by cytometric bead array (CBA) assay determined the polarization of TH1/TH2 responses, whereas H-2 Kb /SIINFEKL tetramers monitored the expansion of OVA-specific T cells. DC-EG7 hybrids stimulated both efficient class I and class II OVA responses, showing that DC-tumor hybrids are also capable of class II cross-presentation. The hybrids also induced the most potent CTLs, offered the highest protection against

established EG7 tumors and also induced the highest stimulation of IFN-gamma and TNF-alpha production. DCs cocultured with irradiated EG7 were also effective at inducing OVA-specific responses, however with slightly reduced potency to those evoked by the hybrids. DCs loaded with lysates Ags were much less efficient at stimulating any of the OVA-specific T-cell responses, showed very little antitumor protection, and stimulated a weak TH1 response, overbalanced by an IL-5 TH2 response. The strategy of Ag-loading clearly influences the ability of DCs to polarize T cells for a TH1/TH2 response and thus determines the outcome of the elicited immune response, during various vaccination protocols.

L7 ANSWER 14 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 7
AN 2004:346071 BIOSIS <<LOGINID::20070522>>
DN PREV200400347202
TI Generation of dendritic cell-tumor cell hybrids by electrofusion for clinical vaccine application.
AU Trevor, Katrina T. [Reprint Author]; Cover, Cathleen; Ruiz, Yvette W.; Akporiaye, Emmanuel T.; Hersh, Evan M.; Landais, Didier; Taylor, Rachel R.; King, Alan D.; Walters, Richard E.
CS Arizona Canc Ctr, 1515 N Campbell Ave,POB 245024, Tucson, AZ, 85748, USA
ktrevor@azcc.arizona.edu
SO Cancer Immunology Immunotherapy, (August 2004) Vol. 53, No. 8, pp. 705-714. print.
CODEN: CIIMDN. ISSN: 0340-7004.
DT Article
LA English
ED Entered STN: 18 Aug 2004
Last Updated on STN: 18 Aug 2004
AB Vaccination with hybrids comprising fused dendritic cells (DCs) and tumor cells is a novel cancer immunotherapy approach designed to combine tumor antigenicity with the antigen-presenting and immune-stimulatory capacities of DCs. For clinical purposes, we have incorporated a large-scale process for the generation of clinical-grade DCs together with novel electrofusion technology. The electrofusion system provides for ease and standardization of method, efficient DC- ***tumor*** ***cell*** ***hybrid*** formation, and large-quantity production of hybrids in a high-volume (6-ml) electrofusion chamber. In addition, we have evaluated DC electrofusion with a variety of allogeneic human tumor cell lines with the rationale that these tumor cell partners would prove a ready, suitable source for the generation of DC- ***tumor*** ***cell*** ***hybrid*** vaccines. The DC production process can generate 6x108 to 2x109 DCs from a single leukapheresis product (apprx180 ml). As determined by FACS analysis, electrofusion of 6x107 total cells (1:1 ratio of DC and tumor cells) resulted in a consistent average of 8-10% DC-tumor cell hybrids, irrespective of the tumor type used. Hybrids were retained in the population for 48 h postfusion and following freezing and thawing. Upon pre-irradiation of the tumor cell partner for vaccine purposes, the overall fusion efficiency was not altered at doses up to 200 Gy. Evaluation of DC- ***tumor*** ***cell*** ***hybrid*** populations for their ability to stimulate T-cell responses demonstrated that electrofused populations are superior to mixed populations of DCs and tumor cells in generating a primary T-cell response, as indicated by IFN-gamma release. Moreover, hybrids comprising HLA-A*0201 DCs and allogeneic melanoma tumor cells (Colo 829 cell line) stimulated IFN-gamma secretion by antigen-specific ***CD8*** + T cells, which are restricted for recognition of a melanoma gp100 peptide antigen (gp100209-217) within the context of the DC HLA haplotype. Maturation of the DC-Colo 829 cell hybrid population served to further improve this T-cell gp100-specific response. Overall, our results are promising for the large-scale generation of electrofused hybrids comprising DCs and allogeneic tumor cells, that may prove useful in human vaccine trials.

L7 ANSWER 15 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8
AN 2004:362645 CAPLUS <<LOGINID::20070522>>
DN 141:87480
TI Destruction of nonimmunogenic mammary ***tumor*** ***cells*** by a ***fusogenic*** oncolytic herpes simplex virus induces potent antitumor immunity
AU Nakamori, Mikihito; Fu, Xinping; Rousseau, Raphael; Chen, Si-Yi; Zhang, Xiaoliu
CS Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX, 77030, USA
SO Molecular Therapy (2004), 9(5), 658-665
CODEN: MTOHCK; ISSN: 1525-0016
PB Elsevier
DT Journal
LA English
AB In principle, destruction of tumor cells in vivo by oncolytic agents would release the entire repertoire of tumor antigens in their natural forms, leading to effective antitumor immunity. This goal has been elusive despite extensive testing of numerous strategies. The authors developed a doubly fusogenic oncolytic herpes simplex virus (Synco-2D) that kills tumor cells by a unique dual mechanism combining direct cytolysis with syncytial formation induced by cell membrane fusion. A single intratumor injection of Synco-2D induced strong antitumor immunity against an otherwise non-immunogenic murine mammary tumor growing in immune-competent mice. ***CD8*** + T cells were the primary mediators of immunity, contributing to the destruction of both primary and metastatic tumors. The authors conclude that the fusogenic capacity of Synco-2D enables it to elicit antitumor immunity exceeding that induced by more conventional oncolytic viruses.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 2004422777 EMBASE <<LOGINID::20070522>>
TI Dendritic cell-based immunotherapy of malignant gliomas.
AU Parajuli P.; Sloan A.E.
CS Dr. P. Parajuli, Department of Neurosurgery, Wayne State University, Karmanos Cancer Institute, 4100 John R. Road, Detroit, MI 48201, United States. pparajuli@neurosurgery.wayne.edu
SO Cancer Investigation, (2004) Vol. 22, No. 3, pp. 405-416. .
Refs: 73
ISSN: 0735-7907 CODEN: CINVD7
CY United States
DT Journal; General Review
FS 008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
ED Entered STN: 28 Oct 2004
Last Updated on STN: 28 Oct 2004
AB The failure of conventional treatment modalities for gliomas, in spite of tremendous progress in research in the past two decades, has led to increasing interest in alternative treatment strategies, including immunotherapy. It has become evident that vaccination with dendritic cells (DC), designed to express tumor antigens, is a potent strategy to elicit anti-tumor immune response in both pre-clinical and clinical settings. Various methods have been applied in order to induce DC to express tumor antigens including: pulsing with isolated tumor peptides or whole tumor lysate; ***fusion*** with ***tumor*** ***cells*** ; and pulsing with apoptotic tumor cells. Herein, we review the recent progress in DC biology with regard to tumor immunity and discuss current DC-based strategies and future prospects in immunotherapy for malignant gliomas.

L7 ANSWER 17 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 9
AN 2005:165500 BIOSIS <<LOGINID::20070522>>
DN PREV200500164675
TI Enhanced antitumor immunity derived from a novel vaccine of fusion hybrid between dendritic and engineered myeloma cells.
AU Hao, Siguo; Bi, Xuguang; Xu, Shuling; Wei, Yangdou; Wu, Xiaochu; Guo, Xuling; Carlsen, Svein; Xiang, Jim [Reprint Author]
CS Hlth Res Div, Saskatchewan Canc Agcy, Saskatoon, SK, S7N 4H4, Canada
JXiang@scf.sk.ca
SO Experimental Oncology, (December 2004) Vol. 26, No. 4, pp. 300-306. print.
ISSN: 1812-9269 (ISSN print).
DT Article
LA English
ED Entered STN: 27 Apr 2005
Last Updated on STN: 27 Apr 2005
AB Aim: Dendritic cell - ***tumor*** ***cell*** ***fusion*** ***hybrid*** vaccines which facilitate antigen presentation represent a new powerful strategy in cancer immunotherapy. The clinical frequency of objective responses to the conventional fusion hybrid vaccines is still quite low, indicating that the current conventional protocol of simply fusing dendritic cells (DCs) and tumor cells needs further improvement to enhance its antitumor efficiency. Methods: In the present study, we generated a novel fusion hybrid DC/J558CD40L by fusing DCs and an engineered J558CD40L myeloma cells expressing CD40 ligand (CD40L) molecule using polyethylene glycol (PEG). The fusion efficiency was approximately 20%. We investigated the antitumor immunity derived from vaccination of the fusion hybrid DC/J558CD40L. Results: Our results showed that vaccination of mice with DC/J558CD40L hybrids induced more efficient cytotoxic T lymphocyte (CTL) responses and protective immunity against J558 tumor cells, than that of the conventional fusion hybrid DC/J558 from the fusion of DCs and J558 tumor cells. The antitumor immunity derived from vaccination of DC/J558CD40L was mainly mediated by CD4+ and ***CD8*** +cT cells, but not natural killer (NK) cells. Conclusion: Therefore, this novel fusion hybrid vaccine which combines gene-modified tumor and DC vaccines may be an attractive strategy for cancer immunotherapy.

L7 ANSWER 18 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:476371 CAPLUS <<LOGINID::20070522>>
DN 141:258953
TI Comparative Analysis of Antigen Loading Strategies of Dendritic Cells for Tumor Immunotherapy
AU Shimizu, Keiji; Kuriyama, Hideyuki; Kjaergaard, Jorgen; Lee, Walter; Tanaka, Hiroshi; Shu, Suyu
CS Center for Surgery Research, The Cleveland Clinic Foundation, Cleveland, OH, USA
SO Journal of Immunotherapy (2004), 27(4), 265-272
CODEN: JOIMF8; ISSN: 1524-9557
PB Lippincott Williams & Wilkins

DT Journal
LA English
AB Dendritic cells (DCs) loaded with antigens can effectively stimulate host immune responses to syngeneic tumors, but there is considerable controversy as to which forms of antigen-loading are most immunogenic. Here, the authors compared immunotherapeutic reactivities of DCs loaded with a variety of antigen prepns. Because DC maturation stages affect their capacities of antigen processing and presentation, two DC populations were used for the current anal.: in vivo Flt-3 ligand-induced mature DCs and in vitro bone marrow-derived DCs, which were less mature. To facilitate a direct comparison, the LacZ gene-transduced B16 melanoma model system was used, where .beta.-galactosidase served as the surrogate tumor-rejection antigen. DC loading strategies included pulsing with the .beta.-galactosidase protein, H-2K restricted peptide, tumor cell lysate, and irradiated ***tumor*** ***cells*** and ***fusion*** of DCs with ***tumor*** ***cells*** . The authors' results demonstrated that electrofusion of DCs and tumor cells generated a therapeutic vaccine far superior to other methods of DC loading. For the treatment of 3-day established pulmonary tumor nodules, a single intranodal vaccination plus IL-12 resulted in a significant redn. of metastatic nodules, while other DC prepns. were only marginally effective. Immunotherapy mediated by the fusion cells was tumor antigen-specific. Consistent with their therapeutic activity, fusion hybrids were the most potent stimulators to induce specific IFN-.gamma. secretion from immune T cells. Furthermore, fusion cells also stimulated a small amt. of IL-10 prodn. from immune T cells. However, this IL-10 secretion was also induced by other DC prepns. and did not correlate with in vivo therapeutic reactivity.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:997244 CAPLUS <<LOGINID::20070522>>
DN 142:91737
TI Therapeutic vaccine generated by electrofusion of dendritic cells and tumour cells
AU Kuriyama, H.; Shimizu, K.; Lee, W.; Kjaergaard, J.; Parkhurst, M. R.; Cohen, P. A.; Shu, S.
CS Center for Surgery Research, The Cleveland Clinic Foundation, Cleveland, OH, USA
SO Developments in Biologicals (Basel, Switzerland) (2004), 116(Development of Therapeutic Cancer Vaccines), 169-178
CODEN: DBEIAI; ISSN: 1424-6074
PB S. Karger AG
DT Journal
LA English
AB Immunotherapy with fusion of dendritic cells (DCs) and tumor cells potentially confers the advantages of DC antigen-presenting functionality and a continuous source of unaltered tumor antigens. However, fusion using chem. or viral fusogens has been inefficient. The authors have recently developed a high throughput electrofusion technique with which very efficient fusion rates (15-54%) were obsd. in over 300 expts., using a variety of murine and human tumor cell lines. The fused cells display a mature DC phenotype and express tumor-assocd. antigens. In two pre-clin. animal models (B16 melanoma transduced with the LacZ gene and the MCA 205
fibrosarcoma), a single vaccination of mice bearing tumors established in the lung, brain and skin resulted in tumor regression and prolongation of life. However, therapeutic efficacy required the administration of adjuvants such as IL-12 and OX-40R mAbs. Effective immunotherapy also required the delivery of fusion cells directly into lymphoid organs (spleen or lymph nodes). Using five defined human T cell lines derived from melanoma patients, allogeneic DCs of HLA-A2, HLA-DR4 and HLA-DR7 haplotypes fused with MART-1, gp100, tyrosinase and TRP-2 expressing 888 mel melanoma cells were analyzed for their ability to stimulate specific cytokine (IFN-.gamma. and GM-CSF) secretion. DC-888 mel hybrids presented all tumor-assocd. epitopes to both CD4 and ***CD8*** T cell lines in the context of MHC class II and I mols., resp. The therapeutic efficacy of a DC-tumor fusion vaccine is now being evaluated for the treatment of metastatic melanoma.
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 10
AN 2003:280092 BIOSIS <<LOGINID::20070522>>
DN PREV200300280092
TI Hybrids of dendritic cells and tumor cells generated by electrofusion simultaneously present immunodominant epitopes from multiple human tumor-associated antigens in the context of MHC class I and class II molecules.
AU Parkhurst, Maria R. [Reprint Author]; DePan, Cormac; Riley, John P.; Rosenberg, Steven A.; Shu, Suyu
CS Surgery Branch, National Cancer Institute, National Institutes of Health, 9000 Rockville Pike, Building 10 Room 2B42, Bethesda, MD, 20892-1502, USA
Maria_Parkhurst@nih.gov
SO Journal of Immunology, (May 15 2003) Vol. 170, No. 10, pp. 5317-5325. print.
ISSN: 0022-1767 (ISSN print).
DT Article
LA English
ED Entered STN: 11 Jun 2003
Last Updated on STN: 11 Jun 2003
AB Hybrid cells generated by ***fusing*** dendritic cells with ***tumor*** ***cells*** (DC-TC) are currently being evaluated as cancer vaccines in preclinical models and human immunization trials. In this study, we evaluated the production of human DC-TC hybrids using an electrofusion protocol previously defined for murine cells. Human DCs were electrically fused with allogeneic melanoma cells (888mel) and were subsequently analyzed for coexpression of unique DC and TC markers using FACS and fluorescence microscopy. Dually fluorescent cells were clearly observed using both techniques after staining with Abs against distinct surface molecules suggesting that true cell fusion had occurred. We also evaluated the ability of human DC-TC hybrids to present tumor-associated epitopes in the context of both MHC class I and class II molecules. Allogeneic DCs expressing HLA-A*0201, HLA-DRbeta1*0401, and HLA-DRbeta1*0701 were fused with 888mel cells that do not express any of these MHC molecules, but do express multiple melanoma-associated Ags. DC-888mel hybrids efficiently presented HLA-A*0201-restricted epitopes from the melanoma Ags MART-1, gp100, tyrosinase, and tyrosinase-related protein 2 as evaluated by specific cytokine secretion from six distinct CTL lines. In contrast, DCs could not cross-present MHC class I-restricted epitopes after exogenously loading with gp100 protein. DC-888mel hybrids also presented HLA-DRbeta1*0401- and HLA-DRbeta1*0701-restricted peptides from gp100 to CD4+ T cell populations. Therefore, ***fusions*** of DCs and ***tumor*** ***cells*** express both MHC class I- and class II-restricted tumor-associated epitopes and may be useful for the induction of tumor-reactive ***CD8*** + and CD4+ T cells in vitro and in human vaccination trials.

L7 ANSWER 21 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2004:152508 BIOSIS <<LOGINID::20070522>>
DN PREV200400147906
TI Characterization of allogeneic leukemia specific CTL from HLA-matched siblings of leukemia patients using dendritic cells-tumor hybrids generated by electrofusion (EF) and polyethylene glycol (PEG) treatment.
AU Re, Francesca [Reprint Author]; Srinivasan, Ramaprasad; Marincola, Franco; Igarashi, Takehito; Barrett, John; Childs, Richard W.
CS Hematology/Bone Marrow Transplant Unit, Institute San Raffaele, Milan, Italy
SO Blood, (November 16 2003) Vol. 102, No. 11, pp. 698a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004
AB INTRODUCTION: The importance of adoptive and innate immunity in mediating
graft versus leukemia effect (GVL) in the field of allogeneic transplantation has become increasingly well known. Harnessing the immune-mediated GVL effect it has led to exploration of strategies in order to elicit an anti-tumor response. In the present study we evaluated the ability to generate allogeneic leukemia-specific CTL in-vitro in an HLA-identical setting by stimulating donor lymphocytes with donor DCs either chemically or electrically fused with patient leukemia cells. METHODS: Leukemia cells were isolated by leukapheresis from the peripheral blood of four patients: 1 acute lymphoid leukemia (ALL), 2 acute myeloid leukemia (AML) and 1 chronic myeloid leukemia (CML). Donor monocyte-derived DCs were fused with patient leukemia cells by using two different techniques: 1) Polyethylene glycol (PEG) was added to a cell pellet containing DCs and tumor cells. 2) Electro-pulsing DCs and tumor cells was accomplished by a pulse of 1000 V/cm at 25 mF. PBMCs from the donors were stimulated in vitro weekly X2 by one of three different populations: 1) irradiated patient ***tumor*** ***cells*** alone 2) electro- ***fused*** DCTH 3) PEG fused DCTH. Donor T cells were then cloned from bulk cultures by limiting dilution and more than one hundred clones were tested for their ability to recognize patient leukemia cells by an ELISA measuring interferon gamma (IFNgamma) secretion or cytotoxicity by Cr51 release. The T-cell population from Limiting Dilution Assay (LDA) was analyzed by FACS. Blocking experiments of antileukemia cytolytic leukemia with monoclonal antibody were performed by preliminary incubation of autologous tumor with anti-pan HLA class I and class II. RESULTS: ***Tumor*** ***cells*** ***fused*** with day 7 DCs were analyzed by dual color fluorescence on FACS for the presence of fusion cells. A fusion efficiency of 5-15% was obtained reproducibility from all separate leukemia patients, either by using chemically or electrically fusion. Donor T cells stimulated by patient leukemia cells typically failed to expand. In contrast, donor T cells stimulated by DCTH proliferated rapidly following each stimulation. While the majority of these clones recognized both leukemia cells and normal patient hematopoietic cells, T cell clones with leukemia specificity were isolated and expanded from all sibling donors. Phenotypic analysis of lymphocytes subpopulation showed that most of the tumor specific T-cell clones were ***CD8*** +, while some of them having a surface marker expression compatible with CD4+ lymphocytes. Moreover there was no significant lysis of K562 and unmatched tumor, thus suggesting an MHC restriction mechanism for tumor killing, as confirmed by blocking

experiments. CONCLUSION: These findings indicate that leukemia specific T-cells as well as T-cells recognizing antigens broadly expressed on haematopoietic cells (i.e. minor histocompatibility antigens) can be generated in-vitro from HLA-matched sibling donors by either chemically or electrically fusing donor DCs to patient tumor. DCTH could be used for the in-vitro expansion of donor T-cells (both CD4+ and ***CD8*** +) with leukemia specificity to be infused post-transplant for future "leukemia targeted" allogeneic transplant trials. Moreover tumor-specific clones generated employing DCTH can potentially be used for the identification of leukemia-specific antigens relevant for tumor rejection.

L7 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:314731 CAPLUS <<LOGINID::20070522>>
DN 136:324056
TI Fusion cells and cytokine compositions for treatment of disease
IN Ohno, Tsuneya
PA USA
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002032378	A2	20020425	WO 2001-US47057	20011022
WO 2002032378	A3	20030227		
WO 2002032378	A9	20030626		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2426366	A1	20020425	CA 2001-2426366	20011022
EP 1368061	A2	20031210	EP 2001-987655	20011022
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511503	T	20040415	JP 2002-535617	20011022
PRAI US 2000-242154P	P	20001020		
WO 2001-US47057	W	20011022		

AB The present invention relates to methods and compns. for treating and preventing cancer and infectious disease by administering a therapeutically ED of fusion cells formed by fusion of autologous dendritic cells and autologous non-dendritic cells, in combination with a cytokine or other mol. which stimulates or induces a cytotoxic T cell response and/or a humoral immune response. The examples discuss cancer vaccines comprising interleukin 12 and dendritic cells ***fused*** with ***tumor*** ***cells*** which induce tumor-specific cytotoxic T-cells. The dendritic cells act as antigen-presenting cells for the tumor-assocd. antigens, thereby inducing tumor-specific immune responses.

L7 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:425324 CAPLUS <<LOGINID::20070522>>
DN 137:19366
TI Method for the production of activated marked tumor-specific T cells for treating cancer
IN Casorati, Giulia; Dellabona, Paolo
PA Science Park RAF S.p.A., Italy
SO U.S., 24 pp., Cont.-in-part of Appl. No. PCT/EP97/01541.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6399054	B1	20020604	US 1998-161998	19980929
WO 9737004	A1	19971009	WO 1997-EP1541	19970326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
PRAI EP 1996-105157	A	19960330		
WO 1997-EP1541	A2	19970326		

AB A method for the prodn. of activated tumor-specific T cells by co-cultivating, ex vivo, tumor cells from a patient with T cells from that patient, comprising the steps of: (i) incubating the ***tumor*** ***cells*** with a first ***fusion*** protein obtained from a B7 protein and one partner of a biol. binding pair and a second fusion protein obtained from an antibody against a cell surface antigen and the other partner of the biol. binding pair, (ii) inhibiting the proliferation of the tumor cells prior to or after that incubation; (iii) co-cultivating the tumor cells with the T cells to be activated, until activation of the T cells is attained; (iv) sepg. the activated T cells from the tumor cells, is highly efficient and can be carried out in a simple manner. Thus, sol. B7-1-IgG1 and B-2-IgG2 costimulate the proliferation of CD4+CD45RO+ human T cells, and induce the acquisition of effector function of ***CD8*** + T cells. Plasmacytoma cells secreting B7-1-IgM, B7-2-IgG3 or B7-2IgG1 mols. induce protective antitumor immunity in syngeneic mice.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 11
AN 2002:547749 BIOSIS <<LOGINID::20070522>>
DN PREV200200547749
TI Recruitment of CTL activity by tumor-specific antibody-mediated targeting of single-chain class I MHC-peptide complexes.
AU Lev, Avital; Novak, Hila; Segal, Dina; Reiter, Yoram [Reprint author]
CS Faculty of Biology, Technion-Israel Institute of Technology, Room 333, Technion City, Haifa, 32000, Israel
reiter@tx.technion.ac.il
SO Journal of Immunology, (September 15, 2002) Vol. 169, No. 6, pp. 2988-2996. print.
CODEN: JOIMA3. ISSN: 0022-1767.
DT Article
LA English
ED Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
AB The MHC class I-restricted ***CD8*** CTL effector arm of the adaptive immune response is uniquely equipped to recognize tumor cells as foreign and consequently initiates the cascade of events resulting in their destruction. However, tumors have developed sophisticated strategies to escape immune effector mechanisms; their most well-known strategy is down-regulation of MHC class I molecules. To overcome this and develop new approaches for immunotherapy, we have constructed a recombinant molecule in which a single-chain MHC is specifically targeted to ***tumor*** ***cells*** through its ***fusion*** to cancer-specific recombinant Ab fragments. As a model we used a single-chain HLA-A2 molecule genetically fused to the variable domains of an anti-IL-2Ralpha subunit-specific humanized Ab, anti-Tac. The construct, termed B2M-aTac(dsFv), was expressed in Escherichia coli, and functional molecules were produced by in vitro refolding in the presence of HLA-A2-restricted antigenic peptides. Flow cytometry studies revealed the ability to decorate Ag-positive, HLA-A2-negative human tumor cells with HLA-A2-peptide complexes in a manner that was entirely dependent upon the specificity of the targeting Ab fragment. Most importantly, the B2M-aTac(dsFv)-mediated coating of the target tumor cells made them susceptible for efficient and specific HLA-A2-restricted, melanoma gp100 peptide-specific CTL-mediated lysis. These results demonstrate the concept that Ab-guided, Ag-specific targeting of MHC-peptide complexes on tumor cells can render them susceptible and more receptive and thus potentiate CTL killing. This type of approach may open the way for the development of new immunotherapeutic strategies based on Ab targeting of natural cognate MHC ligands and CTL-based cytotoxic mechanisms.

L7 ANSWER 25 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 12
AN 2002:515154 BIOSIS <<LOGINID::20070522>>
DN PREV200200515154
TI T-cell blast crisis of chronic myelogenous leukemia manifesting as a large mediastinal tumor.
AU Ye, Charles C.; Echeverri, Carolina; Anderson, Jeanne E.; Smith, Janice L.; Glassman, Armand; Gulley, Margaret L.; Claxton, David; Craig, Fiona E. [Reprint author]
CS Department of Pathology, University of Pittsburgh Medical Center, Presbyterian Hospital, 200 Lothrop St, Room C604, Pittsburgh, PA, 15213, USA
SO Human Pathology, (July, 2002) Vol. 33, No. 7, pp. 770-772. print.
CODEN: HPCQA4. ISSN: 0046-8177.
DT Article
LA English
ED Entered STN: 2 Oct 2002
Last Updated on STN: 2 Oct 2002
AB We report an unusual case of T-cell blast crisis of chronic myelogenous leukemia (CML) with a clinical presentation more typical of de novo T-cell lymphoblastic lymphoma. The patient was a 32-year-old man who presented with acute superior vena cava syndrome 19 months after an initial diagnosis of CML and 5 months after allogeneic bone marrow transplantation. The tumor was composed of primitive lymphoid cells expressing CD2, CD3, CD4, CD5, CD7, ***CD8*** , and CD10. Although the clinical features were more typical of acute lymphoblastic leukemia/lymphoma, fluorescence in situ hybridization analysis showed the bcr-abl ***fusion*** gene within blastic ***tumor*** ***cells*** . This finding confirmed that the mass represented a blastic transformation of CML. We use the unusual features of the current case and the previous reports to suggest that the development of T-cell blast crisis of CML is dependent on the presence of both marrow and extramedullary disease and a mechanism to evade apoptosis.

L7 ANSWER 26 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 13
AN 2003:261147 BIOSIS <<LOGINID::20070522>>
DN PREV200300261147

TI Therapeutic immune response induced by electrofusion of dendritic and tumor cells.
AU Tanaka, Hiroshi; Shimizu, Keiji; Hayashi, Takashi; Shu, Suyu [Reprint Author]
CS Center for Surgery Research, Cleveland Clinic Foundation, 9500 Euclid Avenue, FF50, Cleveland, OH, 44195, USA
shus@ccf.org
SO Cellular Immunology, (November 2002) Vol. 220, No. 1, pp. 1-12. print.
CODEN: CLIMB8. ISSN: 0008-8749.
DT Article
LA English
ED Entered STN: 4 Jun 2003
Last Updated on STN: 4 Jun 2003
AB To elicit a therapeutic antitumor immune response; dendritic cells (DCs) have been employed as a cellular adjuvant. Among various DC-based approaches, ***fusion*** of DCs and ***tumor*** ***cells*** potentially confers not only DC functionality, but also a continuous source of unaltered tumor antigens. We have recently demonstrated successful generation of fusion hybrids by a large-scale electrofusion technique. The immunogenicity and therapeutic potential of fusion hybrids were further analyzed in a model system of a murine melanoma cell line expressing beta-galactosidase (beta-gal) as a surrogate tumor antigen. A single vaccination with fusion hybrids plus IL-12 induced a therapeutic immune response against 3-day established pulmonary metastases. This immunotherapy was beta-gal specific and involved both CD4 and ***CD8*** T cells. In vitro, fusion hybrids stimulated specific IFN-gamma secretion from both CD4 and ***CD8*** immune T cells. They also nonspecifically induced IL-10 secretion from CD4 but not ***CD8*** T cells. Compared to other DC loadings, our results demonstrate the superior immunogenicity of fusion. The current technique of electrofusion is adequately developed for clinical use in cancer immunotherapy.

L7 ANSWER 27 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:242612 CAPLUS <<LOGINID::20070522>>
DN 136:231219
TI ***Tumor*** ***cells*** ***fused*** with dendritic cells for use as antitumor vaccine
IN Gong, Jianxin
PA Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1306859	A	20010808	CN 2000-101792	20000203
PRAI CN 2000-101792		20000203		

AB The antineoplastic vaccine is prepd. by chem., phys. or biol. induced cell fusion between mammalian dendritic cells and mammalian non-dendritic cells at a ratio of 1-25:1. The non-dendritic cells are e.g. breast cancer cells or intestine cancer cells. The chem. fusion method uses polyethylene glycol to induce fusion of dendritic cells and cancer cells cultured in RPMI-1640 or DMEM medium. The phys. fusion method is electrofusion performed in 5% glucose soln. The dendritic cells are derived from bone marrow, peripheral blood or umbilical cord blood; and are cultured in GM-CSF/IL-4-contg. medium. Crude cell mixt. obtained from bone marrow, peripheral blood or umbilical cord blood are pretreated with with anti-CD4, anti- ***CD8*** , and anti-B220/CD45R antibodies, and antibody B21-2, and antibody RB6-8C5 to remove lymphocytes, and nuclear and Ia+ leukocytes.

L7 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:311718 CAPLUS <<LOGINID::20070522>>
DN 135:342905
TI Protective immunity against human carcinoembryonic antigen (CEA) induced by an oral DNA vaccine in CEA-transgenic mice
AU Xiang, Rong; Silletti, Steve; Lode, Holger N.; Dolman, Carrie S.; Ruehlmann, J. Michael; Niethammer, Andreas G.; Pertl, Ursula; Gillies, Stephen D.; Primus, F. James; Reisfeld, Ralph A.
CS Department of Immunology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Clinical Cancer Research (2001), 7(3, Suppl.), 856S-864S
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB Peripheral T-cell tolerance toward human carcinoembryonic self-antigen (CEA) was broken in CEA-transgenic C57BL/6J mice by an oral CEA-based DNA vaccine. This vaccine, delivered by the live, attenuated AroA- strain of Salmonella typhimurium (SL7207), induced tumor-protective immunity mediated by MHC class I-restricted ***CD8*** + T cells. Activation of these T cells was indicated by increased secretion of proinflammatory cytokines IFN-.gamma., interleukin (IL)-12 and granulocyte/macrophage-colony stimulating factor, as well as specific tumor rejection and growth suppression in vaccinated CEA-transgenic mice after a lethal challenge with murine MC38 colon carcinoma cells. These tumor cells were double transfected with CEA and the human epithelial cell adhesion mol. (Ep-CAM)/KSA and consequently served as a docking site for a recombinant antibody-IL2 fusion protein (KS1/4-IL2) recognizing KSA. Importantly, the efficacy of the tumor-protective immune response was markedly increased by boosts with this antibody-IL2 fusion protein, resulting in more effective tumor rejection coupled with increased expression of costimulatory mols. B7.2/B7.2 and intercellular adhesion mol. 1 (ICAM-1) on dendritic cells and intensified release of proinflammatory cytokines IFN-.gamma., IL-12, and granulocyte/macrophage-colony stimulating factor from T cells of successfully vaccinated CEA-transgenic C57BL/6J mice. Increased T-cell activation mediated by boosts with KS1/4-IL2 ***fusion*** protein after ***tumor*** ***cell*** challenge was further indicated by expanded expression of T-cell activation markers CD25, CD28, CD69, and LFA-1. The application of such CEA-based DNA vaccines and its further improved versions may ultimately prove useful in combination therapies directed against human carcinomas expressing CEA self-antigens.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:186844 BIOSIS <<LOGINID::20070522>>
DN PREV200200186844
TI Allogeneic dendritic cells ***fused*** with ***tumor*** ***cells*** : Preclinical results and outcome of a first clinical phase I/II trial in patients with metastatic renal cell carcinoma.
AU Maerten, Angela [Reprint author]; Renoth, Sabine [Reprint author]; Heinicke, Thomas [Reprint author]; von Lilienfeld-Toal, Marie [Reprint author]; Schmidt-Wolf, Ingo G. H. [Reprint author]
CS Dpt. of Internal Medicine I, University of Bonn, Bonn, Germany
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 406a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 13 Mar 2002
Last Updated on STN: 13 Mar 2002
AB Therapeutic vaccination of tumor patients with dendritic cells (DC) can lead to tumor regression in animal models and has shown promising results in first clinical trials in metastatic renal cell carcinoma and malignant melanoma. Here, we present in vitro data and results of a first clinical trial using DC tumor fusion in patients with progressive metastatic renal cell carcinoma. DC precursor cells were obtained from healthy donors from peripheral blood mononuclear cells (PBMCs). DC were fused with either allogeneic or autologous renal tumor cells. In total, twelve patients with progressive metastatic renal cell carcinoma were treated with an average of 2.8X107 ***tumor*** ***cells*** ***fused*** with 1.8X107 DC each administered on days 0, 28 and 56 intradermally. Fusion efficacy was determined for the used tumor cells and was in average 14.3%. Cell viability was 59.8% after fusion and irradiation. Four patients were treated with autologous tumor fusions, eight with allogeneic fusions. We observed no differences comparing these two groups and no adverse effects. Eight patients remained in progressive disease (PD) and four patients showed a stable disease (SD). T cell immunity was carefully monitored before, during and after treatment. DTH reaction using tumor cells was positive after treatment in six out of twelve patients, two of responded with a SD. An increase in the reactivity against recall antigens was seen in most patients. Interestingly, in the group responding with SD, we observed a significant increase of TNF-alpha, in the group with PD a significant decrease of IL-2, IFN-gamma and IL-12 during treatment. Cytotoxicity of PBL increased during treatment as well as interferon gamma secreting cells. We observed an increase of ***CD8*** +CD3+ and CD54+CD3+ and a decrease of T helper cells. Patients with SD showed a significant decrease of CD94 expression. Patients with SD showed significant more CD80+ B cells, CD161+CD56+CD16+CD3- cells and significant less CD94+CD3- cells compared to patients who stayed in PD. The lack of adverse effects together with immunologic effects support further investigation of this novel therapeutic approach. Further studies are necessary to demonstrate clinical effectiveness in tumor patients in particular in patients with less advanced disease.

L7 ANSWER 30 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
AN 2002:152781 BIOSIS <<LOGINID::20070522>>
DN PREV200200152781
TI Characterization of tumor-dendritic cell hybrids generated by electrofusion (EF) and polyethylene glycol (PEG) treatment.
AU Srinivasan, Ramaprasad [Reprint author]; Igarashi, Takehito; Mena, Othon [Reprint author]; Re, Francesca; Fischette, Maria; Takahashi, Yoshiyuki; Carvallo, Cristian [Reprint author]; Young, Neal S.; Linehan, W. Marston [Reprint author]; Childs, Richard W.
CS Medicine and Urologic Oncology Branch, NCI, NIH, Bethesda, MD, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 327b-328b. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 21 Feb 2002

Last Updated on STN: 26 Feb 2002
AB Tumor-dendritic cell (DC) fusions have evoked considerable interest as a means of eliciting tumor-specific cytotoxic T-cell responses. This approach has been utilized for tumor vaccine generation with promising results in a phase I clinical trial. We generated fusions of monocyte-derived DCs with green fluorescent protein (GFP)-transduced tumor cells derived from both hematological malignancies and solid tumors using two different methods-chemical fusion with PEG, and EF. Both techniques yield 10-50% fusion cells as assessed by FACS of unique tumor and DC markers. Due to the potentially toxic nature of the agents employed in inducing cell-cell fusion, we evaluated the viability of tumor cells and DCs after treatment with PEG and electrical pulses. While tumor cells tolerate PEG well, exposure of DCs to PEG under "standard conditions" (50%PEG/10%DMSO/exposure time of 2-5 minutes) triggers cell death (based on FACS for annexin V and 7-AAD positive cells), with the majority of DCs perishing by 24 to 48 hours. Furthermore, cultures of tumor-DC fusion cells (isolated by flow sorting-99% pure) are rapidly outgrown and replaced by tumor cells. In contrast, conditions employed during EF are more permissive for DC survival with DCs subjected to an electrical pulse (1000V/cm, 25 muF) exhibiting survival comparable to untreated controls. Tumor cells, on the other hand, are more susceptible to this treatment, with 40-60% of electrically pulsed tumor cells being non-viable by FACS analysis at 48 hours. Consistent with these findings is the observation that electropulsed and PEG-treated tumor-DC complexes are short lived, with <5% of cells exhibiting both tumor and DC markers at 48 hours. We also investigated tumor fused to DCs under both conditions as well as electropulsed tumor mixed with untreated immature DCs for their ability to stimulate tumor-specific T-cell responses from peripheral blood lymphocytes (PBL) obtained from HLA-matched siblings. ***Tumor*** ***cells*** were either ***fused*** to DCs derived from HLA-identical siblings (donors), or were electropulsed and mixed with untreated donor DCs (EPT/DC) and used to stimulate donor PBL. Bulk T-cell cultures were tested against tumor cells as well as appropriate controls with lymphocyte specificity being inferred from IFN-gamma release as determined by ELISA. Analysis of bulk cultures after two stimulations revealed that electropulsed tumors which were subsequently mixed with untreated DCs were most effective in stimulating tumor-specific T-cell populations, probably as a result of the uptake of dead tumor cells by DCs and subsequent cross-presentation of tumor antigens. Following limiting dilution T-cell cloning, we isolated several tumor-specific ***CD8*** + T cell clones from bulk cultures generated using EPT/DC. These data suggest that generation of stable tumor-DC hybrids is an inefficient process trader the conditions evaluated. We also propose that the impressive clinical efficacy observed in a trial of a tumor-DC vaccine generated by EF derives from cross-priming of T-lymphocytes as a consequence of the uptake of dead tumor cells by autologous DCs. EPT/DC warrants further exploration as a method for the in vitro expansion of leukemia-specific T-cell clones from HLA-matched sibling donors for future use in adoptive immunotherapy strategies following allogeneic peripheral blood stem cell transplants.

L7 ANSWER 31 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
AN 2001:311321 BIOSIS <<LOGINID::20070522>>
DN PREV200100311321
TI T-cells with specificity against neuroblastoma cells activated by dendritic cells.
AU Klein-Franke, A. [Reprint author]; Ertle, F. [Reprint author]; Berkutzky, T. [Reprint author]; Peters, H.
CS Pediatrics, University, Goettingen, Germany
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 41b. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology. CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jun 2001 Last Updated on STN: 19 Feb 2002
AB Introduction: Neuroblastoma is the most frequent solid tumor in children with a poor prognosis despite intensive, multimodal therapy. To improve the outcome new therapeutic approaches are necessary. One new approach in tumor therapy is the activation of cytotoxic T-cells against tumor cells by Dendritic Cells which are by far the most effective Antigen Presenting Cells (APC). Materials and Methods: We used the Neuroblastoma line SK-N-LO and buffy coats of HLA-I matched blood donors as a source for monocytes and T-cells. We isolated the monocytes by plastic adherence and differentiated them into DC by cultivation in the presence of GM-CSF and IL 4 (100 U/ml) and IFN gamma (50 U/ml) for 8 days. Mixed Tumor/Lymphocyte Culture (MLTC) was performed using DC as APC that had either been pulsed with ***tumor*** ***cell*** lysate or ***fused*** to ***tumor*** ***cells*** by PEG. T-cell proliferation was assessed by 3H-Thymidin incorporation and the cytotoxicity of T-cells was monitored via LDH release from tumor cells (4 hours cocultivation, effector:target ratio 10:1). Results: Without DC no activation of T-cells could be seen. In the presence of DC pulsed with tumor cell lysate T-cells were activated leading to a 3H-Thymidin incorporation of 3100 cpm. T-cell activation by DC/tumor cell hybrids was even more efficient yielding 6400 cpm. In both cases ***CD8*** +T-cells were selected and could be kept in continous culture by restimulation with manipulated DC every 14 days, followed by culture in the presence of IL2 for up to four cycles. Freshly activated T-cells lysed 43% of the Neuroblastoma cells, Neuroblastoma cells with different HLA-I formula were not lysed, nor were K562 cells. Lysis of tumor cells was abrogated by a polyclonal rat antibody specific for HLA-I, thus demonstrating the tumor cell lysis to be HLA-I restricted. Discussion: We could activate cytotoxic T-cells against Neuroblastoma cells using Dendritic Cells as APC. Hybrids of DC and tumor cells were even more effective. Target cell lysis was antigen specific, thus the Neuroblastoma cells can be expected to to have tumor associated antigens. Activated T-cells killed Neuroblastoma cells in a HLA-I depentent manner. This is particularly interesting as Neuroblastoma cells bear only very small amounts of HLA-I molecules on their surface. Despite of this Neuroblastoma cells are obviously a suitable target for activated T-cells. These results could lead to clinical studies in the therapy of Neuroblastoma using DC for the activation of tumor specific T-cells.

L7 ANSWER 32 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:17889 CAPLUS <<LOGINID::20070522>>
DN 132:150396
TI Human antigen-presenting cell/tumour cell hybrids stimulate strong allogeneic responses and present tumour-associated antigens to cytotoxic T cells in vitro
AU Dunnion, D. J.; Cywinski, A. L.; Tucker, V. C.; Murray, A. K.; Rickinson, A. B.; Coulie, P.; Browning, M. J.
CS Department of Microbiology and Immunology, Leicester University, Leicester, LE1 9HN, UK
SO Immunology (1999), 98(4), 541-550 CODEN: IMMUAM; ISSN: 0019-2805
PB Blackwell Science Ltd.
DT Journal
LA English
AB Most tumors do not stimulate effective antitumor immune responses in vivo. In order to enhance the immunogenicity of human ***tumor*** ***cells*** , we ***fused*** a variety of ***tumor*** ***cell*** lines with an Epstein-Barr virus transformed B-lymphoblastoid cell line (EBV B-LCL) in vitro, to produce stable hybrid cells. Hybrid cell lines showed a marked increase in their ability to stimulate primary allogeneic T-cell responses in vitro, as compared with the parent tumor cells. The hybrid cells induced proliferation of naive (CD45RA+) as well as memory (CD45RO+) T lymphocytes, and both CD4+ and ***CD8*** + subpopulations of T cells were directly stimulated. The stimulatory hybrids expressed human leukocyte antigen (HLA) class I and II, and a wide range of surface accessory mols., including the T-cell co-stimulatory ligand mols. CD40, CD80 (B7.1) and CD86 (B7.2), the expression of which was required for optimal stimulation of T-cell responses. Fusion of the EBV B-LCL with a melanoma cell line (518.A2) yielded hybrid cells that expressed the melanoma-assocd. antigens MAGE-1 and MAGE-3, and presented these antigens to antigen-specific, HLA class I-restricted cytotoxic T-lymphocyte clones with greater efficiency than the parent melanoma cell line. These findings suggest that the generation of human antigen-presenting cell/tumor cell hybrids offers promise as an approach to cancer immunotherapy.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 33 OF 39 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
AN 1998119789 EMBASE <<LOGINID::20070522>>
TI Gutting edge: Physical interaction between dendritic cells and tumor cells results in an immunogen that induces protective and therapeutic tumor rejection.
AU Celluzzi C.M.; Falo L.D. Jr.
CS Dr. L.D. Falo Jr., Department of Dermatology, Univ. of Pittsburgh Sch. of Medicine, 190 Lothrop Street, Pittsburgh, PA 15213, United States. Lof2@pitt.edu
SO Journal of Immunology, (1 Apr 1998) Vol. 160, No. 7, pp. 3081-3085. . Refs: 30 ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 016 Cancer
026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 7 May 1998 Last Updated on STN: 7 May 1998
AB Dendritic cells (DCs) are potent professional APCs capable of presenting Ag in the context of costimulatory signals necessary for T cell activation. Although tumor cells express target Ags, they are generally incapable of stimulating an immune response. We show that the short term physical interaction of DCs and ***tumor*** ***cells*** , with cell ***fusion*** , results in rapid, efficient, and stable DC tumor cell association. Immunization of naive mice with unselected, irradiated DC-tumor cell conjugates induces tumor, specific ***CD8*** cytotoxic T cells and protection from lethal tumor challenge. Furthermore, the immunogenicity of this cellular vaccine is dependent on the physical interaction of DCs and tumor cells before injection. Immunization with DCs and tumor cells after physical interaction can result in the regression of established tumors and persistent antitumor immunity. These results suggest that immunization, with DCs tumor, cell vaccines may be a simple, rapid and potentistrategy for tumor immunotherapy.

L7 ANSWER 34 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 14
AN 2000:207293 CAPLUS <<LOGINID::20070522>>
DN 133:206421
TI Treatment of hepatocellular carcinoma with the cellular tumor vaccines generated by in vitro modification of tumor cells with non gene transfer approaches
AU Wu, Shuguang; Ma, Jing; Che, Xiaoyan; Liu, Yanjun; Wang, Hao; Zhao, Jian; Shen, Feng; Xie, Tainpei; Trojan, Jerzy; Wu, Mengchao; Guo, Yajun
CS Institute of Pharmacology and Biotechnology, The First Military Medical University Guangzhou, Canton, 510515, Peop. Rep. China
SO Advances in Experimental Medicine and Biology (1998), 451(Gene Therapy of Cancer), 283-293
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Press
DT Journal; General Review
LA English
AB A review with 30 refs. Antitumor immune responses are mediated primarily by T cells. Down regulation of MHC and the mols. that costimulate the immune responses is assocd. with defective signaling of tumor cells for T cell activation. In vitro ***fusion*** of autologous ***tumor*** ***cells*** with antigen presenting cells (APCs) or treatment of tumor cells with a combination of cytokines increased the expression of MHC class I and adhesion mols. on tumor cell surfaces that costimulate host immune responses. The hybrid cells generated by ***fusion*** of ***tumor*** ***cells*** with APCs and the tumor cells treated in vitro with a combination of cytokines and pre-incubated with a bispecific monoclonal antibody (bi-Mab) crosslinking antigen on tumor cells to CD28 on T cells, become immunogenic and able to stimulate naive T cells with generation of tumor specific cytotoxic T cells both in vitro and in vivo. Immunization with the modified tumor cells elicits an immune response mediated by both CD4+ and ***CD8*** + T cells. This response protected against a parental tumor cell challenge and cured established tumors. The approach was effective in both low immunogenic and non-immunogenic tumor systems. Modification of ***tumor*** ***cells*** with tumor:APC ***fusion*** or the 2-step procedure may provide a strategy for development of tumor vaccines that is effective for cancer immunotherapy.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:679163 CAPLUS <<LOGINID::20070522>>
DN 127:318114
TI Method for the production of activated marked tumor-specific T cells and use thereof in treatment of tumors
IN Casorati, Giulia; Dellabona, Paolo
PA Boehringer Mannheim G.m.b.h., Germany; Casorati, Giulia; Dellabona, Paolo
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9737004	A1	19971009	WO 1997-EP1541	19970326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2250394	A1	19971009	CA 1997-2250394	19970326
AU 9721602	A	19971022	AU 1997-21602	19970326
EP 914416	A1	19990512	EP 1997-914312	19970326
EP 914416	B1	20020612		
R: DE, ES, FR, GB, IT				
JP 2000515364	T	20001121	JP 1997-534912	19970326
ES 2177964	T3	20021216	ES 1997-914312	19970326
US 6399054	B1	20020604	US 1998-161998	19980929
PRAI EP 1996-105157	A	19960330		
WO 1997-EP1541	W	19970326		

AB A method for the prodn. of activated tumor-specific T cells by co-cultivating, ex vivo, tumor cells from a patient with T cells from that patient, comprising the steps of: i) incubating the ***tumor*** ***cells*** with a first ***fusion*** protein obtained from a B7 protein and one partner of a biol. binding pair and a second fusion protein obtained from an antibody against a cell surface antigen and the other partner of the biol. binding pair; ii) inhibiting the proliferation of the tumor cells prior to or after that incubation; iii) co-cultivating the tumor cells with the T cells to be activated, until activation of the T cells is attained; i.v.) sepg. the activated T cells from the tumor cells, is highly efficient and can be carried out in a simple manner. Demonstrated were costimulation of human CD4+CD45R0+ T lymphocytes by recombinant sol. B7-1Ig and B7-2Ig mols., costimulation of ***CD8*** + T cells against allogeneic tumor by sol. B7-1IgG1 and interleukin 2, induction of antitumor immunity by plasmacytoma cells secreting B7-1Ig or B7-2Ig mols., etc.

L7 ANSWER 36 OF 39 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:315481 CAPLUS <<LOGINID::20070522>>
DN 127:32753
TI Costimulation of T cell proliferation by a chimeric B7-2 antibody fusion protein specifically targeted to cells expressing the erbB2 proto-oncogene
AU Gerstmayer, Bernhard; Altenschmidt, Uwe; Hoffmann, Michael; Wels, Winfried
CS Inst. Experimental Cancer Research, Tumor Biology Center, Freiburg, D-79106, Germany
SO Journal of Immunology (1997), 158(10), 4584-4590
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB T cells require at least 2 signals for activation and clonal expansion. The first signal conferring specificity is initiated by interaction of the T cell receptor with antigenic peptides in the context of MHC mols. The second, costimulatory signal can be provided by cell surface mols. on APCs such as B7-1 (***CD8***) and B7-2 (CD86), which interact with their counter-receptors on T cells. The absence of costimulatory signals presents one possible mechanism for tumor cells to escape immune surveillance. In exptl. models transfection of B7 genes into tumor cells can result in T cell-dependent tumor rejection. The authors developed a novel approach to direct the costimulatory B7-2 mol. to the surface of target cells. Their approach is based on a chimeric fusion protein that consists of the extracellular domain of human B7-2 fused to a single-chain Ab domain (scFv) specific for the ErbB2 protein, a type I growth factor receptor overexpressed in a high percentage of human adenocarcinomas. This B7-2225-scFv(FRP5) mol. expressed in the yeast Pichia pastoris and purified from culture supernatants is functionally active and binds to B7 counter-receptors and to ErbB2. B7-2225-scFv(FRP5) localizes specifically to the surface of ErbB2-expressing target cells, thereby providing a costimulatory signal that results in enhanced proliferation of syngeneic T cells. Effective tumor vaccines for cancer immunotherapy thus could be created by targeting such chimeric ligands to the surface of tumor cells.
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L7 ANSWER 37 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 15
AN 1997:253260 BIOSIS <<LOGINID::20070522>>
DN PREV199799552463
TI Induction of antitumor activity by immunization with fusions of dendritic and carcinoma cells.
AU Gong, Jianlin; Chen, Dongshu; Kashiwaba, Masahiro; Kufe, Donald
CS Div. Cancer Pharmacol., Dana-Farber Cancer Inst., Harv. Med. Sch., 44 Binney St., Boston, MA 02115, USA
SO Nature Medicine, (1997) Vol. 3, No. 5, pp. 558-561.
ISSN: 1078-8956.
DT Article
LA English
ED Entered STN: 13 Jun 1997
Last Updated on STN: 13 Jun 1997
AB Dendritic cells (DCs) are potent antigen-presenting cells that prime naive cytotoxic T-cells (CTLs). In this study, we have fused DCs with MC38 carcinoma cells. The fusion cells were positive for major histocompatibility (MHC) class I and II, costimulating molecules and intercellular cell adhesion molecule-1 (ICAM-1). The results show that the fusion cells stimulate naive T cells in the primary mixed lymphocyte reaction (MLR) and induce MC38 tumor-specific CTLs in vivo. Antibody-mediated depletion experiments demonstrate that induction of CD4+ and ***CD8*** + CTLs protects against challenge with tumor cells. We also show that immunization with the fusion cells induces rejection of established metastases. These findings represent the first demonstration that ***fusions*** of DCs and ***tumor*** ***cells*** can be used in the treatment of cancer.

L7 ANSWER 38 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 16
AN 1997:306332 BIOSIS <<LOGINID::20070522>>
DN PREV199799614135
TI Antitumor vaccination with gene-transduced ***tumor*** ***cells*** expressing a ***fusion*** protein RM4/IFN-itoa.
AU Xiang, Jim
CS Saskatoon Cancer Cent., 20 Campus Drive, Saskatoon, Saskatchewan S7N 4H4, Canada
SO Cancer Biotherapy and Radiopharmaceuticals, (1997) Vol. 12, No. 2, pp. 123-130.
ISSN: 1084-9785.
DT Article
LA English
ED Entered STN: 26 Jul 1997
Last Updated on STN: 26 Jul 1997
AB Our previous studies showed that secretion of a fusion protein RM4/IFN-tau from a mouse myeloma cell line V-KC-K/RM4-IFN-tau curtailed its tumorigenicity. Inoculation of V-KC-K/RM4-IFN-tau tumor cells further induced a protective immunity against a secondary challenge of parental V-KC-K tumor cells, in which the predominant immune cellular components are ***CD8*** + T cells. In this study, V-KC-K/RM4-IFN-tau cell line was again used to further characterize the protective immunity. We found that the reduced tumorigenicity of V-KC-K/RM4-IFN-tau was directly related

to the amount of ***fusion*** protein secreted by ***tumor*** ***cells*** , and that ***CD8*** + T cells derived from mice experienced with V-KC-K/RM4-IFN-tau tumor regression played an important role in the protective immunity in a chromium release assay in vitro and in an animal study in vivo by using T-cell subset depleted mice. Our animal studies also showed that not only the cytotoxic but also the memory T-cells against the secondary challenge of parental V-KC-K cells could be adoptively transferred to normal BALB/c mice. In addition, our animal studies further showed that local vaccination of irradiated V-KC-K/RM4-IFN-tau cells was able to significantly inhibit established tumors in early stages in vivo. This study thus highlights the potential utility of this engineered V-KC-K/RM4-IFN-tau ***tumor*** ***cells*** secreting the ***fusion*** protein RM4/IFN-tau in cancer gene therapy.

L7 ANSWER 39 OF 39 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 17
AN 1994:130604 BIOSIS <<LOGINID::20070522>>
DN PREV199497143604
TI Effective tumor vaccine generated by fusion of hepatoma cells with activated B cells.
AU Guo, Yajun [Reprint author]; Wu, Mengchao [Reprint author]; Chen, Hen [Reprint author]; Wang, Xiaoning [Reprint author]; Liu, Guangluo [Reprint author]; Li, Guanglo [Reprint author]; Ma, Jing; Sy, Man-Sun
CS Tumor Immunol. Biotherapy Center, Eastern Inst. Hepatobiliary Surg., Shanghai 200433, China
SO Science (Washington D C), (1994) Vol. 263, No. 5146, pp. 518-520. CODEN: SCIEAS. ISSN: 0036-8075.
DT Article
LA English
ED Entered STN: 24 Mar 1994
Last Updated on STN: 24 Mar 1994
AB Fusion of BERH-2 rat hepatocellular carcinoma cells with activated B cells produced hybrid cells that lost their tumorigenicity and became immunogenic. Syngeneic rats injected with BERH-2-B hybrid cells became resistant to challenge with parental BERH-2 cells, and rats with established BERH-2 hepatomas were cured by subsequent injection of BERH-2-B cells. Both CD4+ and ***CD8*** + cells were essential for the induction of protective immunity; however, only ***CD8*** + cells were required for the eradication of BERH-2 tumors. The generation of ***hybrid*** ***tumor*** ***cells*** that elicit antitumor immune responses may be a useful strategy for cancer immunotherapy.

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